

What is claimed is:

1. A method of producing particles comprising the steps of:
providing a load stock comprising:
an excipient that is a solid at 25°C and 1 atmosphere pressure;
and
optionally, a biologically active substance;
contacting the load stock with a supercritical fluid to form a melt;
expanding the melt across a pressure drop to form solid particles
comprising the load stock that are simultaneously dispersed,
foamed and cooled to a temperature below 25°C; and
reducing the average particle size of the solid particles using a milling
device.
2. The method according to claim 1 further comprising the steps of:
freezing at least a portion of the supercritical fluid during the expanding
step to form frozen fluid particles;
using the frozen fluid particles during the reducing step as a milling
media for the solid particles comprising the load stock.
3. The method according to claim 1 wherein the load stock further
comprises a solvent.
4. The method according to claim 3 wherein the solvent is an
organic solvent.
5. The method according to claim 3 further comprising extracting
the solvent from the melt using supercritical fluid as an extracting agent prior
to the expanding step.

6. The method according to claim 1 wherein the reducing step accomplished by a means selected from the group consisting of milling, grinding, comminuting, micronizing, pulverizing and jetting.

7. The method according to claim 1 wherein subsequent to the reducing step the solid particles have an average particle size of from about 0.1 to about 500 micrometers (μm).

8. The method according to claim 1 wherein the excipient is a polymer selected from the group consisting of polysaccharides, polyesters, polyethers, polyanhydrides, polyglycolides, polylactic acids, polycaprolactones, polyethylene glycols and polypeptides.

9. The method according to claim 1 wherein the supercritical fluid is selected from the group consisting of carbon dioxide, water, nitrous oxide, dimethylether, straight chain or branched C1-C6-alkanes, alkenes, alcohols, ethane, propane, fluoroform, chlorotrifluoromethane, chlorodifluoromethane, propylene, ammonia and combinations thereof.

10. The method according to claim 1 wherein the supercritical fluid is carbon dioxide.

11. A plurality of particles produced according to the method of claim 1.

12. An apparatus for producing solid particles comprising:
a vessel for receiving a load stock comprising:
an excipient that is a solid at 25°C and 1 atmosphere pressure;
and
optionally, a biologically active substance;
a supercritical fluid supply in fluid communication with the vessel;

control means for selectively flowing supercritical fluid from the supercritical fluid supply to the vessel to transform the load stock to a melt;
an expansion chamber;
a nozzle in fluid communication between the vessel and the expansion chamber for expanding the expanding across a pressure drop to form solid particles comprising the load stock that are cooled to a temperature below 25°C; and
a milling device in fluid communication with the expansion chamber for reducing the average particle size of the solid particles before the temperature of the solid particles is permitted to rise to or above 25°C.

13. A method of producing particles comprising the steps of:
providing a load stock comprising:
an excipient that is a solid at 25°C and 1 atmosphere pressure;
and
optionally, a biologically active substance;
contacting the load stock with a supercritical fluid in a pressure vessel to form a melt;
releasing the pressure within the pressure vessel to transform the melt into a solid porous mass that is cooled to a temperature below 25°C; and
milling the solid porous mass to obtain solid particles.

14. The method according to claim 13 wherein the solid porous mass is milled before the temperature of the solid porous mass is permitted to rise to or above 25°C.

15. The method according to claim 13 wherein subsequent to the reducing step the solid particles have an average particle size of from about 0.1 to about 500 micrometers (μm).

16. The method according to claim 13 wherein the excipient is a polymer selected from the group consisting of polysaccharides, polyesters, polyethers, polyanhydrides, polyglycolides, polylactic acids, polycaprolactones, polyethylene glycols and polypeptides.

17. The method according to claim 13 wherein the supercritical fluid is selected from the group consisting of carbon dioxide, water, nitrous oxide, dimethylether, straight chain or branched C1-C6-alkanes, alkenes, alcohols, ethane, propane, fluoroform, chlorotrifluoromethane, chlorodifluoromethane, propylene, ammonia and combinations thereof.

18. The method according to claim 13 wherein the supercritical fluid is carbon dioxide.

19. A plurality of particles produced according to the method of claim 13.